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| 08/170,344 | 03/30/94 | KAST | W D45113TFM |

| EXAMINER |
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| MINNIFIELD |

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| ART UNIT | PAPER NUMBER |
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| 1813 | 8 |

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NEW YORK, NY 10112

DATE MAILED: 10/04/94

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 7-18-94 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

**Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:**

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☒ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ ______

**Part II SUMMARY OF ACTION**

1. ☒ Claims 1-24 are pending in the application.

   Of the above, claims ______ are withdrawn from consideration.

2. ☒ Claims 23 have been cancelled.
3. ☐ Claims ______ are allowed.
4. ☒ Claims 1-22, 24 are rejected.
5. ☐ Claims ______ are objected to.
6. ☐ Claims ______ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on ______. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on ______. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed ______, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. ______ ; filed on ______.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

## Part III DETAILED ACTION

### *Response to Amendment*

15. Applicants' amendments filed April 17, 1995 and May 14, 1995 are acknowledged and have been entered. Claim 3 has been cancelled. Claims 1, 2, and 16-21 have been amended. Claims 1, 2, 4-22, and 24 are now pending in the present application. All prior rejections are withdrawn with the exception of those discussed below.

16. The text of the 35 U.S.C. Code not included in this Office Action can be found in the prior Office Action.

17. The information disclosure statement filed January 4, 1994 fails to comply with 37 CFR § 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in § 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicants state (April 17, 1995) that a substitute IDS will be filed, however it has not been received.

18. The objection to the specification and rejection of claims 1, 2, 4-22, and 24 under 35 U.S.C. § 112, first paragraph (i.e. lack of an enabling disclosure) is maintained. This rejection is maintained for essentially the same reasons as the rejection of claims 1-22 and 24 under this statutory provision, as set forth in paragraphs 17 and 18 of the last Office action. Applicants' arguments filed April 17,1995 have been fully considered but they are not deemed to be persuasive.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure. The disclosure is enabled for nonapeptide sequences from the E6 or E7 genes of HPV16 or HPV18, and MHC Class I molecules as specifically taught in the specification. The specification has not provided sufficient evidence of a method of prophylactic or therapeutic treatment of a human with cervical carcinoma or other HPV related diseases by administering a peptide from HPV proteins in a pharmaceutical composition. Matlashewski et al. discloses that HPV18 proteins (E6 gene) maybe diagnostically useful since the proteins have been identified in specific human cancers, however the methods as claimed in this invention are not known in the art. Accordingly, amendment of the claims to what is supported in the specification or filing of evidence in the form of a Rule 132 declaration providing factual evidence supporting the broad range claims is suggested.

A disclosure in an application, to be complete, must contain such description and details as to enable any person skilled in the art or science to which it pertains to make and use the invention as of its filing date, In re Glass, 181 USPQ 31; 492 F2.d 1228 (CCPA 1974). While the prior art setting may be mentioned in general terms, the essential novelty, the essence of the invention, must be described in such details, including proportions and techniques where necessary, as to enable those persons skilled in the art to make and utilize the invention.

Specific operative embodiments or examples of the invention must be set forth. Examples and description should be of sufficient scope as to justify the scope of the claims. Where the constitution and formula of a compound is stated only as probability and speculation, the disclosure is not sufficient to support claims identifying the compound by such composition or formula. A disclosure involving a new chemical compound or composition must teach persons skilled in the art how to make the

compound. Incomplete teachings may not be completed by reference to subsequently filed applications.

The instant specification invites the skilled artisan to experiment. The factor which must be considered in determining undue experimentation are set forth in Ex parte Forman 230 USPQ 546. The factors include 1) quantity of experimentation necessary, 2) the amount of guidance presented, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the predictability of the art and the 7) breath of the claims. With regard to factors three and six, it is noted that there are no working examples or support for in vivo efficacy of the active ingredients in a method of prophylactic or therapeutic treatment of a human with cervical carcinoma or other HPV related diseases by administering a peptide from HPV proteins in a pharmaceutical composition, or peptides from any HPV that bind to MHC Class I molecules. Such is not seen as sufficient to support the breath of the claims, wherein the scope of the claims encompasses how to prepare a peptide from any of the listed HPV proteins (or any other HPV protein) wherein the peptide binds to any human MHC Class I molecule. It is noted that Law requires that the disclosure of an application shall inform those skilled in the art how to use applicant's alleged discovery, not how to find out how to use it for themselves., see In re Gardner et al. 166 USPQ 138 (CCPA 1970).

Applicants have argued that the specification is enabled and have cited Ruppert et al., Kast et al., Feltkamp et al., Vitiello et al., and Ressing et al. as support to demonstrate enablement, however it is noted that the specification must be enabled as of its filing date. Prior art references that were published after Applicants' effective filing date (5-5-92) cannot be used to rebut prima facie case of nonenablement under 35 USC 112. In re Glass, 181 USPQ 31; 492 F2.d 1228 (CCPA 1974).

Applicants have argued that it would be unethical to demonstrate HPV treatment in humans, however the Examiner has not suggested such a demonstration. Applicants have not demonstrated treatment of HPV in animal models. With regard

to the method of prophylactic or therapeutic treatment, it appears that the specification is a paper protocol. The specification does not show any therapy or prophylatic treatment, only in vitro studies; no animal studies using the peptides to demonstrate prophylatic or therapy treatment that would correlate to human efficacy have been set forth in the specification.

Applicants have argued that Kast et al. (1991, PNAS 88:2283-2287 and 1991, Immunol. Letters 30(2):229-232) show that one of skill in the art would readily understand from these references how to make and use the claimed invention. Kast et al. (1991, PNAS) disclose the immunization of synthetic peptides of Sendai virus, not HPV. Further, Kast et al. (1991, Immunol. Letters) does disclose the use of peptide vaccination, however the use of HPV peptides is not discussed. HPV is discussed with regard to using "... cultured human CTL for immunotherapy of virus-induced tumors" (p. 229). Furthermore, the reference discloses that there are several unanswered questions regarding peptide vaccination as a novel immnuotherapeutic or preventive approach in man (summary; p. 230, col. 2).

In response to Applicant's argument that Matlashewski et al. does not include certain features of Applicant's invention, the limitations on which the Applicant relies (i.e., peptides that bind in the groove on top of an MHC Class I molecule) are not stated in the claims. Therefore, it is irrelevant whether the reference includes those features or not.

19. The rejection of claims 1, 2, 4, 7, 8, 11, 13, and 15-23 under 35 U.S.C. § 102(b) as anticipated by, or in the alternative, under 35 U.S.C. § 103 as obvious over Schoolnik et al. is maintained. This rejection is maintained for essentially the same reasons as the rejection of claims 1-22 and 24 under this statutory provision, as set forth in paragraph 24 of the last Office action. Applicants' arguments filed April 17, 1995 have been fully considered but they are not deemed to be persuasive.

Schoolnik et al. discloses synthetic peptides from HPV that are useful in the diagnosis and therapy of conditions associated with HPV infection (abstract; p. 9, l. 10-18; claims). Schoolnik et al. teaches the preparation of peptides from HPV16 (E6 and E7) or other HPV proteins useful to raise antibodies for diagnostic, protective (i.e. prophylactic), and therapeutic purposes and vaccines, as well as various mode of administration (p. 3, l. 1-39; p. 5, l. 28-50; p. 4, l. 27 to p. 5, l. 24; p. 7, l. 47 to p. 8, l. 8).

It is noted that the claims recite a peptide comprising an amino acid sequence from a protein of E6 or E7 of HPV 16 or HPV 18.

The teachings of Schoolnik et al. anticipates the claimed invention by disclosing a peptide from a HPV protein wherein the peptide binds to a MHC Class I molecule, and a method of prophylactic or therapeutic treatment of a human with cervical carcinoma or other HPV related diseases by administering a peptide from HPV proteins in a pharmaceutical composition. The compositions and methods disclosed in Schoolnik et al. are believed to inherently possess properties which anticipates the claimed invention or if they are not the same the composition and methods, the HPV peptides (and compositions) and methods of treatment as disclosed by Schoolnik et al. would none the less render the claims obvious because it possesses the components necessary to prepare a peptide from HPV and methods of treatment as claimed in the instant application. Binding of MHC Class I molecules via T-cell activation is an inherent part of the process of generating an immunogenic response in a mammal. Since the Office does not have the facilities for examining and comparing applicants' method for preparation of a HPV peptide and methods of treatment of the prior art, the burden is on applicant to show a novel or unobvious differences between the claimed product and the product of the prior art (i.e., that the peptide, composition, and method of use of the prior art does not possess the same material structural and functional characteristics of the claimed composition and methods of preparation).

See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

In response to Applicant's argument that Schoolnik et al. does not include certain features of Applicant's invention, the limitations on which the Applicant relies (i.e., peptides have to fit snugly in the groove of HLA Class I molecule; pockets in the groove; specific anchor residues) are not stated in the claims. Therefore, it is irrelevant whether the reference includes those features or not.

It is noted that the use of prior art published after Applicants' effective filing date can not be used rebut rejections.

20. The following new rejection has not been necessitated by the amendment.

21. Claims 5, 6, 8, 10, 12, and 14 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are indefinite for being in improper Markush format. The Office recommends the use of the phrase "selected from the group consisting of..." with the use of the conjunction "and" rather than "or" in listing the species. See MPEP 706.03(Y).

OK, clerk needs to correct.

22. No claims are allowed.

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is (703) 305-3394. The examiner can normally be reached on Monday-Thursday from 7:00 AM-4:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christine M. Nucker, can be reached on (703) 308-4028. The fax phone number for this Group is (703) 305-7939.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

N. M. Minnifield
August 21, 1995

HAZEL F. SIDBERRY
PRIMARY EXAMINER
GROUP 1800